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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,430	BOHMER, RALPH M.	
	Examiner	Art Unit	
	GAILENE R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2008 and 24 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 58-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 58-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment filed May 14, 2008 and response, filed March 24, 2008, are acknowledged and have been entered. Claims 16-57 have been cancelled. Claims 58-68 have been added. Claims 1-4, 6-12, 14, and 15 have been amended. Accordingly, claims 1-15 and 58-68 are pending. Claims 1-15 and 58-68 are under examination.

Withdrawn Rejections / Objections

2. All rejections or objections not reiterated herein, have been withdrawn.

3. In light of Applicant's amendment and arguments, the rejection of claims 5, 7-9 and 11-13 under 35 U.S.C. 102(b) as being anticipated by Warwick et al. (Detection strategy for maternal antibodies against paternal HPA-1 antigen, The Lancet 344: page 64 (July 2, 1994)), is hereby, withdrawn.

4. In light of Applicant's amendment and arguments, the rejection of claims 5, 7-9, and 11-13 under 35 U.S.C. 102(b) as being anticipated by Bussel et al. (Antenatal Treatment of Neonatal Alloimmune Thrombocytopenia, The New England Journal of Medicine 319:1374-1378 (November 24, 1988)), is hereby, withdrawn.

5. In light of Applicant's amendment and arguments, the rejection of claims 1-5, 7-9 and 11-15 under 35 U.S.C. 103(a) as being unpatentable over Simons (US Patent 5,447,842) in view of Warwick et al. (The Lancet 344: page 64 (July 2, 1994)) or Bussel

et al. (The New England Journal of Medicine 319:1374-1378 (November 24, 1988)), is hereby, withdrawn.

6. In light of Applicant's amendment and arguments, the rejections of claims 6 and 10 under 35 U.S.C. 103(a) as being unpatentable over Simons (US Patent 5,447,842) in view of Warwick et al. (The Lancet 344: page 64 (July 2, 1994)) or Bussel et al. (The New England Journal of Medicine 319:1374-1378 (November 24, 1988)) as applied to claims 1-5, 7-9 and 11-15 above, and further in view of Tsang et al. (Optimum dissociating condition for immunoaffinity and preferential isolation of antibodies with high specific activity, Journal of Immunological Methods 138: 291- 299 (1991)) and also Sisson et al. (An Improved Method for immobilizing IgG antibodies on protein A-agarose, Journal of Immunological Methods 127:215-220 (1990)), respectively, are hereby, withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 58-60, 63, and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58, steps i)-iii) are confusing in relation to claim 1 from which claim 58 depends because it is unclear how steps i)-iii) functionally and cooperatively relate to

the method steps recited in claim 1. If steps i)-iii) are intended to be performed in a specific order congruous to the method steps in claim 1, steps a) and b), i.e. as an example: a) - i) - ii) - b) - iii); then such should be clearly defined to render the instant claim definite.

Claim 58 step ii) is confusing in relation to step i) because it is unclear what essential functional cooperative relationship exists between the fetal cells in step ii) and the isolated PBMC in step i). Are the fetal cells parts of the isolated fraction in step i)?

Claim 59, is also confusing in relation to claims 1 and 58 from which it depends because claim 1 and 58 appear to recite that the maternal antibodies being detected are those that physiologically bound in vivo to the paternally inherited fetal antigen present in the fetal cells. Specifically, independent claim 1 calls for identifying a fetal cell present in maternal blood sample which carries paternally inherited fetal antigen by way of detecting maternal antibody present in the maternal blood sample that bound to the fetal cell carrying the paternally inherited fetal antigen. Accordingly, it is unclear why maternal antibodies against paternally inherited fetal antigen are being "added in vitro" to the peripheral blood mononuclear cells (PBMC). Accordingly, claim 59 also lacks clear antecedent basis for the recitation of "the isolated PBMC." See also claim 62.

Claim 60 is ambiguous in reciting "depleting… of at least one type of maternal cell" because it fails to define what "at least one type of maternal cell" is being depleted, and its functional relationship with the fetal cell being isolated.

Claim 63 is vague and indefinite in reciting, "isolatable label", because it is unclear what is encompassed in the term "isolatable" in terms of labels as used in the claim.

Claim 65 is vague and indefinite in reciting, "separating a fraction comprising the label" because it is unclear what is encompassed in the recitation of "a fraction comprising the label" as recited in the claim. Does Applicant intend "a fraction comprising the label bound to the complexes formed?

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-15 and 58-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the

amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for identifying a fetal cell from maternal blood, wherein fetal cell-maternal antibody complexes are identified and recovered. The maternal antibody is specific for paternally inherited fetal antigen present in the fetal cells, and the maternal antibody-bound fetal complexes are identified using a secondary antibody or other molecule that binds to the maternal antibody.

The state of the prior art- the prior art of record fails to disclose a method for identifying a fetal cell carrying paternally inherited fetal antigen present in maternal blood, using an antibody that binds to the maternal antibody that is complexed with fetal cell carrying the paternally inherited fetal antigen.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed secondary antibody will specifically and exclusively detect and identify fetal cell-maternal antibody complexes that specifically consist of fetal cells carrying the paternally inherited fetal antigen.

The amount of direction or guidance present- appropriate guidance is provided in the specification for the claimed method to work using the secondary antibody in binding and identifying a broad spectrum of human immunoglobulins or antibodies present in maternal blood plasma. However, the specification fails to provide guidance to enable the claimed method to function in exclusively detecting and identifying the fetal cell-

maternal antibody complexes that specifically consist of fetal cells carrying the paternally inherited fetal antigen in maternal blood, as claimed.

The presence or absence of working examples- working examples are provided in the specification that show using the secondary antibody in binding and identifying a broad spectrum of human immunoglobulins or antibodies present in maternal blood plasma. There are no working examples that show analogous results in exclusively detecting and identifying the fetal cell-maternal antibody complexes that specifically consist of fetal cells carrying the paternally inherited fetal antigen in maternal blood, as claimed.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to use the method as claimed, to specifically and exclusively identify fetal cells carrying paternally inherited fetal antigen present in maternal blood for purposes of isolating and enriching such rare fetal cells.

The breadth of the claims- as recited, the instant claims are directed to a method for identifying and enriching fetal cells from maternal blood, wherein fetal cell-maternal antibody complexes are identified and recovered using a secondary antibody or other molecule that binds to maternal and human antibodies.

The invention is drawn to a method for identifying and enriching fetal cells from maternal blood, wherein fetal cell-maternal antibody complexes are identified and recovered. Applicant's disclosure at page 6, last full paragraph provides that the maternal antibodies are bound to fetal cells (in vivo) at time of blood collection due to fetal cell exposure to maternal plasma at the time the fetal cells cross-over into maternal

plasma. Alternatively, maternal antibodies may also be bound in vitro by contacting cells derived from maternal PBMC with antibody-containing fraction of maternal plasma for a time and under conditions sufficient to permit formation of maternal antibody-bound fetal complexes (page 7, second and third full paragraph). Applicant then discloses that the maternal antibodies that comprise the maternal antibody-bound fetal cell complexes to be detected and identified are those that are specific for paternally inherited fetal antigen present in the fetal cells, and they are identified using a secondary antibody or other molecule or "isolatable agent" that is capable of binding to the maternal antibody (page 7, fourth full paragraph).

The claims specifically recite that maternal antibody is 1) specific for paternally inherited fetal antigen present in fetal cells, or 2) specifically bound to paternally inherited fetal antigen present in the fetal cells, and it is that maternal antibody that is detected and identified in the claimed method.

In page 14, fourth full paragraph, however, the agent disclosed that is intended to bind maternal antibodies bound to fetal cells which specifically carry paternally inherited fetal antigen are antibodies or fragments thereof that bind generally to human antibodies or polypeptides that bind human antibodies such as protein A, protein G, and protein L, and deemed to be isolatable. Human antibodies encompass all of anti-human IgG, IgM, and all other immunoglobulins. Although it is stated that the agent, preferably, does not bind molecules in maternal blood other than maternal antibody, nowhere in the specification discloses a particular agent having the level of specific binding to maternal

antibody that is specifically bound to fetal cell, much less a fetal cell carrying the paternally inherited fetal antigen, as claimed.

General statements are also provided in page 14, last full paragraph, which the antibody may be polyclonal or monoclonal and that preferably the antibody is monoclonal antibody; and that monoclonal antibodies can be raised in one species against an immunoglobulin from another the binding sites of antibodies of another species. Applicant provides that the monoclonal antibodies having antigen binding specificity can be generated using known conventional techniques in the art. Although it is stated that a particularly preferred agent is an anti-idiotypic antibody that binds to a maternal antibody that is specific for a paternal antigen and it can be generally isolated from maternal blood as immune complexes comprising the maternal antibody and the anti-idiotypic antibody (page 15), the specification does not show any working examples exemplifying use of anti-idiotypic secondary antibody having the level of specific binding to maternal antibody that is specifically bound to fetal cell, much less a fetal cell carrying the paternally inherited fetal antigen, as claimed.

The fact that the claimed method may appear to work based on proof of principle regarding existence of maternal anti-fetal antibodies, it is not sufficient to enable the breadth of the claimed invention. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification.

Patent protection is granted in return for enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1996), stating in context of the utility requirement that "a patent is not a hunting license. It is not a reward for the search, but for compensation for its successful conclusion." Tossing out the mere germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by the inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Genentech Inc. v. Novo Nordisk A/A (CAFC) 42 USPQ2d 1001.

Response to Arguments

8. Applicant's arguments with respect to claims 1-15 have been considered but are moot in view of the new grounds of rejection.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday to Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

September 29, 2008